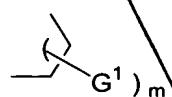


wherein

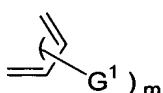
R^1 and R^2 :

- i) independently represent H or lower alkyl;
- ii) together form a bridge of structure



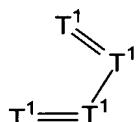
wherein bonding is achieved via the terminal carbon atoms;

- iii) together form a bridge of structure



wherein bonding is achieved via the terminal carbon atoms; or

- iv) together form a bridge of structure



wherein one or two ring members T^1 are N and the others are CH, and bonding is achieved via the terminal atoms; and

wherein

m is 0 or an integer 1 – 4; and

G^1 is a substituent independently selected from the group consisting of

- $-N(R^6)_2$;
- $-NR^3COR^6$;
- halogen;
- alkyl;
- cycloalkyl;

- AX*
- Sub B*
- lower alkenyl;
 - lower cycloalkenyl;
 - halogen-substituted alkyl;
 - amino-substituted alkyl;
 - N-lower alkylamino-substituted alkyl;
 - N,N-di-lower alkylamino-substituted alkyl;
 - N-lower alkanoylamino-substituted alkyl;
 - hydroxy-substituted alkyl;
 - cyano-substituted alkyl;
 - carboxy-substituted alkyl;
 - lower alkoxycarbonyl-substituted alkyl;
 - phenyl lower alkoxycarbonyl-substituted alkyl;
 - halogen-substituted alkylamino;
 - amino-substituted alkylamino;
 - N-lower alkylamino-substituted alkylamino;
 - N,N-di-lower alkylamino-substituted alkylamino;
 - N-lower alkanoylamino-substituted alkylamino;
 - hydroxy-substituted alkylamino;
 - cyano-substituted alkylamino;
 - carboxy-substituted alkylamino;
 - lower alkoxycarbonyl-substituted alkylamino;
 - phenyl-lower alkoxycarbonyl-substituted alkylamino;
 - -OR⁶;
 - -SR⁶;
 - -S(O)R⁶;
 - -S(O)₂R⁶;
 - halogenated lower alkoxy;
 - halogenated lower alkylthio;
 - halogenated lower alkylsulfonyl;
 - -OCOR⁶;
 - -COR⁶;

- S U b
β /*
- X*
- -CO₂R⁶;
 - -CON(R⁶)₂;
 - -CH₂OR³;
 - -NO₂;
 - -CN;
 - amidino;
 - guanidino;
 - sulfo;
 - -B(OH)₂;
 - optionally substituted aryl;
 - optionally substituted heteroaryl;
 - optionally substituted saturated heterocyclyl;
 - optionally substituted partially unsaturated heterocyclyl;
 - -OCO₂R³;
 - optionally substituted heteroarylalkyl;
 - optionally substituted heteroaryloxy;
 - -S(O)_p(optionally substituted heteroaryl);
 - optionally substituted heteroarylalkyloxy;
 - -S(O)_p(optionally substituted heteroarylalkyl);
 - -CHO;
 - -OCON(R⁶)₂;
 - -NR³CO₂R⁶;
 - -NR³CON(R⁶)₂

R³ is H or lower alkyl;

R⁶ is independently selected from the group consisting of

- H;
- alkyl;
- optionally substituted aryl;
- optionally substituted aryl lower alkyl; and

Sub B1

R⁴ is H, halogen, or lower alkyl;

p is 0, 1, or 2;

X is selected from the group consisting of O, S, and NH;

Y is selected from the group consisting of

- -(CR⁴)_n-S(O)_p-(5-membered heteroaryl)-(CR⁴)_s-;
- -(CR⁴)_n-C(G²)(R⁴)-(CR⁴)_s-;

wherein

n and s are each independently 0 or an integer of 1 – 2; and

G² is selected from the group consisting of -CN, -CO₂R³, -CON(R⁶)₂, and
-CH₂N(R⁶)₂;

- -O-CH₂-;
- -S(O)-;
- -S(O)₂-;
- -SCH₂-;
- -S(O)CH₂-;
- -S(O)₂CH₂-;
- -CH₂S(O)-; and
- -CH₂S(O)₂-

A and D independently represent N or CH;

B and E independently represent N or CH;

L represents N or CH;

with the provisos that

- a) the total number of N atoms in the ring containing A, B, D, E, and L is 1, 2, or 3;
and
- b) when L represents CH, at least one of A and D is an N atom;

q is 0, 1, or 2;

*Sub
β1*

η1

G^3 is selected from the group consisting of

- lower alkyl;
- $-NR^3COR^6$;
- carboxy-substituted alkyl;
- lower alkoxy carbonyl-substituted alkyl;
- $-OR^6$;
- $-SR^6$;
- $-S(O)R^6$;
- $-S(O)_2R^6$;
- $-OCOR^6$;
- $-COR^6$;
- $-CO_2R^6$;
- $-CH_2OR^3$;
- $-CON(R^6)_2$;
- $-S(O)_2N(R^6)_2$;
- $-NO_2$;
- $-CN$;
- optionally substituted aryl;
- optionally substituted heteroaryl;
- optionally substituted saturated heterocyclyl;
- optionally substituted partially unsaturated heterocyclyl;
- optionally substituted heteroarylalkyl;
- optionally substituted heteroaryloxy;
- $-S(O)_p$ (optionally substituted heteroaryl);
- optionally substituted heteroarylalkyloxy;
- $-S(O)_p$ (optionally substituted heteroarylalkyl);
- $-OCON(R^6)_2$;
- $-NR^3CO_2R^6$;
- $-NR^3CON(R^6)_2$;

J is a ring selected from the group consisting of

- aryl;
- pyridyl; and
- cycloalkyl;

Sub B1
A/1

q' represents the number of substituents G⁴ on ring J and is 0, 1, 2, 3, 4, or 5, and

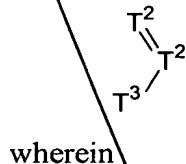
G⁴ moieties are selected from the group consisting of

- -N(R⁶)₂;
- -NR³COR⁶;
- halogen;
- alkyl;
- cycloalkyl;
- lower alkenyl;
- lower cycloalkenyl;
- halogen-substituted alkyl;
- amino-substituted alkyl;
- N-lower alkylamino-substituted alkyl;
- N,N-di-lower alkylamino-substituted alkyl;
- N-lower alkanoylamino-substituted alkyl;
- hydroxy-substituted alkyl;
- cyano-substituted alkyl;
- carboxy-substituted alkyl;
- lower alkoxycarbonyl-substituted alkyl;
- phenyl lower alkoxycarbonyl-substituted alkyl;
- halogen-substituted alkylamino;
- amino-substituted alkylamino;
- N-lower alkylamino-substituted alkylamino;
- N,N-di-lower alkylamino-substituted alkylamino;
- N-lower alkanoylamino-substituted alkylamino;
- hydroxy-substituted alkylamino;
- cyano-substituted alkylamino;

- SUV
V31
R/
- carboxy-substituted alkylamino;
 - lower alkoxycarbonyl-substituted alkylamino;
 - phenyl-lower alkoxycarbonyl-substituted alkylamino;
 - -OR⁶;
 - -SR⁶;
 - -S(O)R⁶;
 - -S(O)₂R⁶;
 - halogenated lower alkoxy;
 - halogenated lower alkylthio;
 - halogenated lower alkylsulfonyl;
 - -OCOR⁶;
 - -COR⁶;
 - -CO₂R⁶;
 - -CON(R⁶)₂;
 - -CH₂OR³;
 - -NO₂;
 - -CN;
 - amidino;
 - guanidino;
 - sulfo;
 - -B(OH)₂;
 - optionally substituted aryl;
 - optionally substituted heteroaryl;
 - optionally substituted saturated heterocyclyl;
 - optionally substituted partially unsaturated heterocyclyl;
 - -OCO₂R³;
 - optionally substituted heteroarylalkyl;
 - optionally substituted heteroaryloxy;
 - -S(O)_p(optionally substituted heteroaryl);
 - optionally substituted heteroarylalkyloxy;
 - -S(O)_p(optionally substituted heteroarylalkyl);

- -CHO;
- -OCON(R⁶)₂;
- -NR³CO₂R⁶;
- -NR³CON(R⁶)₂
- fused ring-forming bridges attached to and connecting adjacent positions of ring J, said bridges having the structures:

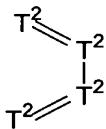
a)



wherein

each T² independently represents N, CH, or CG⁴;T³ represents S, O, CR⁴G⁴, C(R⁴)₂, or NR³; andbonding to ring J is achieved via terminal atoms T² and T³;

b)



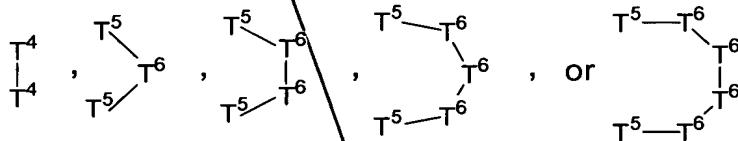
wherein

each T² independently represents N, CH, or CG⁴;with the proviso that a maximum of two bridge atoms T² may be N ;

and

bonding to ring J is achieved via terminal atoms T²; and

c)



wherein

each T⁴, T⁵, and T⁶ independently represents O, S, CR⁴G⁴, C(R⁴)₂, or NR³; andbonding to ring J is achieved via terminal atoms T⁴ or T⁵ ;

with the provisos that:

i) when one T⁴ is O, S, or NR³, the other T⁴ is CR⁴G⁴ or C(R⁴)₂ ;

- ii) a bridge comprising T⁵ and T⁶ atoms may contain a maximum of two heteroatoms O, S, or N; and
- iii) in a bridge comprising T⁵ and T⁶ atoms, when one T⁵ group and one T⁶ group are O atoms, or two T⁶ groups are O atoms, said O atoms are separated by at least one carbon atom;

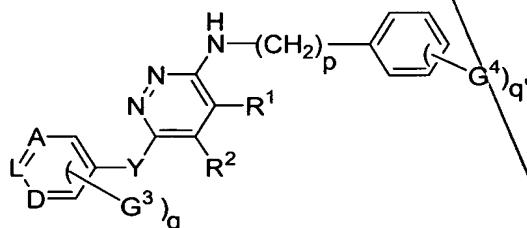
A
Sub B

and with the further provisos that:

- in G¹, G², G³, and G⁴, when two groups R⁶ are each alkyl and located on the same N atom they may be linked by a bond, an O, an S, or NR³ to form a heterocycle of 5 – 7 ring atoms; and
- when an aryl, heteroaryl, or heterocyclyl ring is optionally substituted, that ring may bear up to 5 substituents which are independently selected from the group consisting of amino, mono-loweralkyl-substituted amino, di-loweralkyl-substituted amino, lower alkanoylamino, halogeno, lower alkyl, halogenated lower alkyl, hydroxy, lower alkoxy, lower alkylthio, halogenated lower alkoxy, halogenated lower alkylthio, lower alkanoyloxy, -CO₂R³, -CHO, -CH₂OR³, -OCO₂R³, -CON(R⁶)₂, -OCO N(R⁶)₂, -NR³CON(R⁶)₂, nitro, amidino, guanidino, mercapto, sulfo, and cyano;

or a pharmaceutically acceptable salt or prodrug thereof.

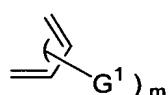
2. (amended) A compound having the structural formula



wherein

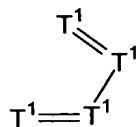
R¹ and R² :

- i) together form a bridge of structure



wherein bonding is achieved via the terminal carbon atoms; or

ii) together form a bridge of structure



wherein one of the ring members T¹ is N and the others are CH, and bonding is achieved via the terminal atoms; and

wherein

m is 0 or an integer 1 – 2; and

*G*¹ is a substituent independently selected from the group consisting of

- -N(R⁶)₂;
- -NR³COR⁶;
- halogen;
- alkyl;
- amino-substituted alkylamino;
- N-lower alkylamino-substituted alkylamino;
- N,N-di-lower alkylamino-substituted alkylamino;
- N-lower alkanoylamino-substituted alkylamino;
- hydroxy-substituted alkylamino;
- carboxy-substituted alkylamino;
- lower alkoxycarbonyl-substituted alkylamino;
- -OR⁶;
- -SR⁶;
- -S(O)R⁶;
- -S(O)₂R⁶;
- halogenated lower alkoxy;
- halogenated lower alkylthio;
- halogenated lower alkylsulfonyl;
- -OCOR⁶;
- -COR⁶;
- -CO₂R⁶;

*Sub
β1*

A/

- Sub B1*
- -CON(R⁶)₂ ;
 - -NO₂ ;
 - -CN;
 - optionally substituted heteroarylalkyl;
 - optionally substituted heteroaryloxy;
 - -S(O)_p(optionally substituted heteroaryl);
 - optionally substituted heteroarylalkyloxy;
 - -S(O)_p(optionally substituted heteroarylalkyl);

R³ is H or lower alkyl;

A1

R⁶ is independently selected from the group consisting of

- H;
- lower alkyl;
- optionally substituted aryl;
- optionally substituted aryl lower alkyl; and

p is 0 or 1;

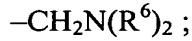
Y is selected from the group consisting of

- -(CH₂)_n-S(O)_p-(5-membered heteroaryl)-(CH₂)_s-;
- -(CH₂)_n-C(G²)(H)-(CH₂)_s- ;

wherein

n and s are each independently 0 or 1; and

G² is selected from the group consisting of -CN, -CO₂R³, -CON(R⁶)₂, and



- -O-CH₂- ;
- -S(O)- ;
- -S(O)₂- ;
- -SCH₂- ;
- -S(O)CH₂- ;

- $-\text{S}(\text{O})_2\text{CH}_2-$;
- $-\text{CH}_2\text{S}(\text{O})-$; and
- $-\text{CH}_2\text{S}(\text{O})_2-$

A and D independently represent N or CH;

L represents N or CH;

with the provisos that

- Sub B1*
- a) the total number of N atoms in the ring containing A, D, and L is 1 or 2; and
 - b) when L represents CH, at least one of A and D is an N atom;

AN

q is 0, 1, or 2;

G^3 is selected from the group consisting of

- lower alkyl;
- $-\text{NR}^3\text{COR}^6$;
- $-\text{OR}^6$;
- $-\text{SR}^6$;
- $-\text{S}(\text{O})\text{R}^6$;
- $-\text{S}(\text{O})_2\text{R}^6$;
- $-\text{CO}_2\text{R}^6$;
- $-\text{CON}(\text{R}^6)_2$;
- $-\text{S}(\text{O})_2\text{N}(\text{R}^6)_2$;
- $-\text{CN}$;
- optionally substituted aryl;
- optionally substituted heteroaryl;
- optionally substituted heteroarylalkyl;
- optionally substituted heteroaryloxy;
- $-\text{S}(\text{O})_p(\text{optionally substituted heteroaryl})$;
- optionally substituted heteroarylalkyloxy;
- $-\text{S}(\text{O})_p(\text{optionally substituted heteroarylalkyl})$;

Sub P1
A1

~~q'~~ represents the number of substituents G^4 on the phenyl ring and is 0, 1, 2, or 3;

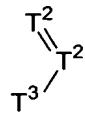
and

G^4 moieties are selected from the group consisting of

- $-N(R^6)_2$;
- $-NR^3COR^6$;
- halogen;
- alkyl;
- halogen-substituted alkyl;
- hydroxy-substituted alkyl;
- carboxy-substituted alkyl;
- lower alkoxy carbonyl-substituted alkyl;
- amino-substituted alkylamino;
- N-lower alkylamino-substituted alkylamino;
- N,N-di-lower alkylamino-substituted alkylamino;
- N-lower alkanoylamino-substituted alkylamino;
- hydroxy-substituted alkylamino;
- carboxy-substituted alkylamino;
- lower alkoxy carbonyl-substituted alkylamino;
- phenyl-lower alkoxy carbonyl-substituted alkylamino;
- $-OR^6$;
- $-SR^6$;
- $-S(O)R^6$;
- $-S(O)_2R^6$;
- halogenated lower alkoxy;
- halogenated lower alkylthio;
- halogenated lower alkylsulfonyl;
- $-OCOR^6$;
- $-COR^6$;
- $-CO_2R^6$;
- $-CON(R^6)_2$;
- $-CH_2OR^3$;

- Sch B1*
- -NO₂;
 - -CN;
 - optionally substituted heteroarylalkyl;
 - optionally substituted heteroaryloxy;
 - -S(O)_p(optionally substituted heteroaryl);
 - optionally substituted heteroarylalkyloxy;
 - -S(O)_p(optionally substituted heteroarylalkyl);
 - fused ring-forming bridges attached to and connecting adjacent positions of the phenyl ring, said bridges having the structures:

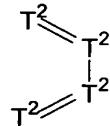
a)



wherein

each T² independently represents N, CH, or CG⁴;T³ represents S, O, CHG⁴, CH₂, or NR³; andbonding to the phenyl ring is achieved via terminal atoms T² and T³;

b)



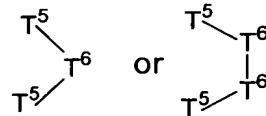
wherein

each T² independently represents N, CH, or CG⁴;with the proviso that a maximum of two bridge atoms T² may be N ;

and

bonding to the phenyl ring is achieved via terminal atoms T²; and

c)



wherein

each T⁵, and T⁶ independently represents O, S, CHG⁴, CH₂, or NR³; and
bonding to the phenyl ring is achieved via terminal atoms T⁵ ;

with the provisos that:

- i) a bridge comprising T⁵ and T⁶ atoms may contain a maximum of two heteroatoms O, S, or N; and
- ii) in a bridge comprising T⁵ and T⁶ atoms, when one T⁵ group and one T⁶ group are O atoms, or two T⁶ groups are O atoms, said O atoms are separated by at least one carbon atom;

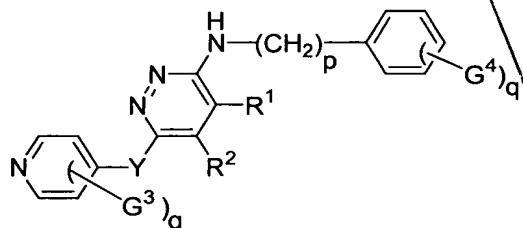
*Sub
p1*

and with the further provisos that:

- in G¹, G², G³, and G⁴, when two groups R⁶ are each alkyl and located on the same N atom they may be linked by a bond, an O, an S, or NR³ to form a heterocycle of 5 – 7 ring atoms; and
- when an aryl, heteroaryl, or heterocyclyl ring is optionally substituted, that ring may bear up to 2 substituents which are independently selected from the group consisting of amino, mono-loweralkyl-substituted amino, di-loweralkyl-substituted amino, lower alkanoylamino, halogeno, lower alkyl, halogenated lower alkyl, hydroxy, lower alkoxy, lower alkylthio, halogenated lower alkoxy, halogenated lower alkylthio, lower alkanoyloxy, -CO₂R³, -CH₂OR³, -OCO₂R³, -CON(R⁶)₂, -OCO N(R⁶)₂, -NR³CON(R⁶)₂, nitro, and cyano;

or a pharmaceutically acceptable salt or prodrug thereof.

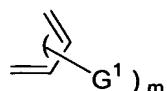
3. (amended) A compound having the structural formula



wherein

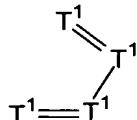
R¹ and R² :

- i) together form a bridge of structure



wherein bonding is achieved via the terminal carbon atoms, and any group G¹ is located on a non-terminal atom of the bridge; or

- ii) together form a bridge of structure



wherein one of the ring members T¹ is N and the others are CH, and bonding is achieved via the terminal atoms; and

wherein

m is 0 or an integer 1 – 2; and

Sub B1

G¹ is a substituent independently selected from the group consisting of

- -N(R⁶)₂;
- -NR³COR⁶;
- halogen;
- -OR⁶ wherein R⁶ represents lower alkyl;
- -NO₂;
- optionally substituted heteroaryloxy;
- optionally substituted heteroarylalkyloxy;

R³ is H or lower alkyl;

R⁶ is independently selected from the group consisting of

- H;
- lower alkyl;
- optionally substituted aryl;
- optionally substituted aryl lower alkyl; and

p is 0 or 1;

Y is selected from the group consisting of

- Sub B1*
- $-\text{S(O)}_p\text{-}(5\text{-membered heteroaryl})\text{-}$;
 - $-\text{C}(\text{CN})(\text{H})\text{-}$;
 - $-\text{O-CH}_2\text{-}$;
 - $-\text{S(O)}\text{-}$; and
 - $-\text{S(O)}_2\text{-}$;

q is 0 or 1;

G³ is selected from the group consisting of

- lower alkyl;
- $-\text{NR}^3\text{COR}^6$;
- $-\text{CO}_2\text{R}^6$;
- $-\text{CON}(\text{R}^6)_2$;
- $-\text{S(O)}_2\text{N}(\text{R}^6)_2$;

q' represents the number of substituents G⁴ on the phenyl ring and is 0, 1, 2, or 3;

and

G⁴ moieties are selected from the group consisting of

- $-\text{N}(\text{R}^6)_2$;
- halogen;
- lower alkyl;
- halogen-substituted lower alkyl;
- $-\text{OR}^6$;
- $-\text{SR}^6$;
- $-\text{S(O)R}^6$;
- $-\text{S(O)}_2\text{R}^6$;
- halogenated lower alkoxy;
- halogenated lower alkylthio;
- halogenated lower alkylsulfonyl;
- $-\text{OCOR}^6$;
- $-\text{COR}^6$;

- Sub B1*
- A/B*
- N-lower alkanoylamino-substituted alkyl;
 - hydroxy-substituted alkyl;
 - cyano-substituted alkyl;
 - carboxy-substituted alkyl;
 - lower alkoxycarbonyl-substituted alkyl;
 - phenyl lower alkoxycarbonyl-substituted alkyl;
 - halogen-substituted alkylamino;
 - amino-substituted alkylamino;
 - N-lower alkylamino-substituted alkylamino;
 - N,N-di-lower alkylamino-substituted alkylamino;
 - N-lower alkanoylamino-substituted alkylamino;
 - hydroxy-substituted alkylamino;
 - cyano-substituted alkylamino;
 - carboxy-substituted alkylamino;
 - lower alkoxycarbonyl-substituted alkylamino;
 - phenyl-lower alkoxy carbonyl-substituted alkylamino;
 - -OR⁶;
 - -SR⁶;
 - -S(O)R⁶;
 - -S(O)₂R⁶;
 - halogenated lower alkoxy;
 - halogenated lower alkylthio;
 - halogenated lower alkylsulfonyl;
 - -OCOR⁶;
 - -COR⁶;
 - -CO₂R⁶;
 - -CON(R⁶)₂;
 - -CH₂OR³;
 - -NO₂;
 - -CN;
 - amidino;

- Sub
B1
A3*
- guanidino;
 - sulfo;
 - -B(OH)2 ;
 - optionally substituted aryl;
 - optionally substituted heteroaryl;
 - optionally substituted saturated heterocyclyl;
 - optionally substituted partially unsaturated heterocyclyl;
 - -OCO₂R³;
 - optionally substituted heteroarylalkyl;
 - optionally substituted heteroaryloxy;
 - -S(O)_p(optionally substituted heteroaryl);
 - optionally substituted heteroarylalkyloxy;
 - -S(O)_p(optionally substituted heteroarylalkyl);
 - -CHO;
 - -OCON(R⁶)₂ ;
 - -NR³CO₂R⁶ ;
 - -NR³CON(R⁶)₂

R³ is H or lower alkyl;

R⁶ is independently selected from the group consisting of

- H;
- alkyl;
- optionally substituted aryl;
- optionally substituted aryl lower alkyl; and

R⁴ is H, halogen, or lower alkyl;

p is 0, 1, or 2;

X is selected from the group consisting of O, S, and NH;

Sub B1

Y is selected from the group consisting of

- lower alkylene, optionally substituted by OH or OAcyl;
 - -CH₂-O- ;
 - -CH₂-S- ;
 - -CH₂-NH- ;
 - -O- ;
 - -S- ;
 - -NH- ;
 - -(CR⁴)_n-S(O)_p-(5-membered heteroaryl)-(CR⁴)_s-;
 - -(CR⁴)_n-C(G²)(R⁴)-(CR⁴)_s- ;
- A3*
- wherein

n and s are each independently 0 or an integer of 1 – 2; and

G² is selected from the group consisting of -CN, -CO₂R³, -CON(R⁶)₂, and
-CH₂N(R⁶)₂ ;

- -O-CH₂- ;
- -S(O)- ;
- -S(O)₂- ;
- -SCH₂- ;
- -S(O)CH₂- ;
- -S(O)₂CH₂- ;
- -CH₂S(O)- ; and
- -CH₂S(O)₂-

A and D independently represent N or CH;

B and E independently represent N or CH;

L represents N or CH;

with the provisos that

- a) the total number of N atoms in the ring containing A, B, D, E, and L is 1, 2, or 3;
and
- b) when L represents CH, at least one of A and D is an N atom;

Sub B1

q is 0, 1, or 2;

A3

G^3 is selected from the group consisting of

- $-NR^3COR^6$;
- carboxy-substituted alkyl;
- lower alkoxy carbonyl-substituted alkyl;
- $-OR^6$;
- $-SR^6$;
- $-S(O)R^6$;
- $-S(O)_2R^6$;
- $-OCOR^6$;
- $-COR^6$;
- $-CO_2R^6$;
- $-CH_2OR^3$;
- $-CON(R^6)_2$;
- $-S(O)_2N(R^6)_2$;
- $-NO_2$;
- $-CN$;
- optionally substituted aryl;
- optionally substituted heteroaryl;
- optionally substituted saturated heterocyclyl;
- optionally substituted partially unsaturated heterocyclyl;
- optionally substituted heteroarylalkyl;
- optionally substituted heteroaryloxy;
- $-S(O)_p$ (optionally substituted heteroaryl);
- optionally substituted heteroarylalkyloxy;
- $-S(O)_p$ (optionally substituted heteroarylalkyl);
- $-OCON(R^6)_2$;
- $-NR^3CO_2R^6$;
- $-NR^3CON(R^6)_2$;

J is a ring selected from the group consisting of

- aryl;
- pyridyl; and
- cycloalkyl;

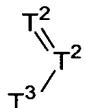
q' represents the number of substituents G⁴ on ring J and is 0, 1, 2, 3, 4, or 5, and

G⁴ moieties are selected from the group consisting of

- Sub 13*
- -N(R⁶)₂;
 - -NR³COR⁶;
 - halogen;
 - alkyl;
 - cycloalkyl;
 - lower alkenyl;
 - lower cycloalkenyl;
 - halogen-substituted alkyl;
 - amino-substituted alkyl;
 - N-lower alkylamino-substituted alkyl;
 - N,N-di-lower alkylamino-substituted alkyl;
 - N-lower alkanoylamino-substituted alkyl;
 - hydroxy-substituted alkyl;
 - cyano-substituted alkyl;
 - carboxy-substituted alkyl;
 - lower alkoxycarbonyl-substituted alkyl;
 - phenyl lower alkoxycarbonyl-substituted alkyl;
 - halogen-substituted alkylamino;
 - amino-substituted alkylamino;
 - N-lower alkylamino-substituted alkylamino;
 - N,N-di-lower alkylamino-substituted alkylamino;
 - N-lower alkanoylamino-substituted alkylamino;
 - hydroxy-substituted alkylamino;
 - cyano-substituted alkylamino;

- Sub B1*
- $-\text{CO}_2\text{R}^6;$
 - $-\text{CON}(\text{R}^6)_2;$
 - $-\text{CH}_2\text{OR}^3;$
 - $-\text{NO}_2;$
 - $-\text{CN};$
 - optionally substituted heteroarylalkyl;
 - optionally substituted heteroaryloxy;
 - $-\text{S(O)}_p(\text{optionally substituted heteroaryl});$
 - optionally substituted heteroarylalkyloxy;
 - $-\text{S(O)}_p(\text{optionally substituted heteroarylalkyl});$
 - fused ring-forming bridges attached to and connecting adjacent positions of the phenyl ring, said bridges having the structures:

a)



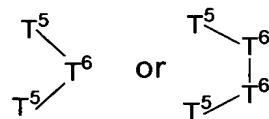
wherein

each T^2 independently represents N, CH, or CG^4 ;

T^3 represents S, O, CHG^4 , CH_2 , or NR^3 ; and

bonding to the phenyl ring is achieved via terminal atoms T^2 and T^3 ;

b)



wherein

each T^5 , and T^6 independently represents O, S, CHG^4 , CH_2 , or NR^3 ; and

bonding to the phenyl ring is achieved via terminal atoms T^5 ;

with the provisos that:

- i) a bridge comprising T^5 and T^6 atoms may contain a maximum of two heteroatoms O, S, or N; and
- ii) in a bridge comprising T^5 and T^6 atoms, when one T^5 group and one T^6 group are O atoms, or two T^6 groups are O atoms, said O atoms are separated by at least one carbon atom;

and with the further provisos that:

- in G¹, G², G³, and G⁴, when two groups R⁶ are each alkyl and located on the same N atom they may be linked by a bond, an O, an S, or NR³ to form a heterocycle of 5 – 6 ring atoms; and

A1

- when an aryl, heteroaryl, or heterocyclyl ring is optionally substituted, that ring may bear up to 2 substituents which are independently selected from the group consisting of amino, mono-loweralkyl-substituted amino, di-loweralkyl-substituted amino, lower alkanoylamino, halogeno, lower alkyl, halogenated lower alkyl, hydroxy, lower alkoxy, lower alkylthio, halogenated lower alkoxy, halogenated lower alkylthio, -CO₂R³, -CON(R⁶)₂, nitro, and cyano;

or a pharmaceutically acceptable salt or prodrug thereof.

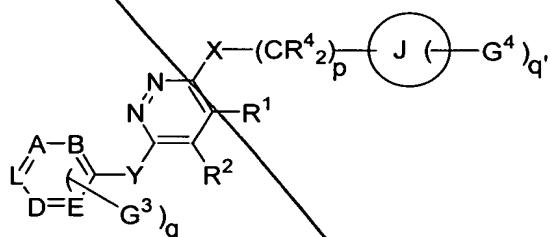
A2 B1

5. (Amended) A method of treating a mammal having a condition of tumor growth, retinopathy, rheumatoid arthritis, psoriasis, or a bullous disorder associated with subepidermal blister formation, comprising administering to said mammal an amount of a compound of claim 1 which is effective to treat said condition.

6. (cancelled) The method of claim 5, wherein said condition is tumor growth; retinopathy, including diabetic retinopathy, ischemic retinal-vein occlusion, retinopathy of prematurity, and age-related macular degeneration; rheumatoid arthritis; psoriasis; or a bullous disorder associated with subepidermal blister formation, including bullous pemphigoid, erythema multiforme, and dermatitis herpetiformis.

7. (amended) A compound having the structural formula

A3
Sub
B1

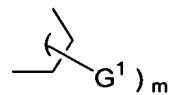


wherein

Sub B1

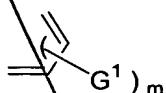
R¹ and R²:

- i) independently represent H or lower alkyl;
- ii) together form a bridge of structure



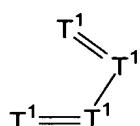
wherein bonding is achieved via the terminal carbon atoms;

- iii) together form a bridge of structure



wherein bonding is achieved via the terminal carbon atoms; or

- iv) together form a bridge of structure



wherein one or two ring members T¹ are N and the others are CH, and bonding is achieved via the terminal atoms; and

wherein

m is 0 or an integer 1 – 4; and

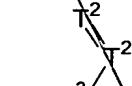
G¹ is a substituent independently selected from the group consisting of

- -N(R⁶)₂;
- -NR³COR⁶;
- halogen;
- alkyl;
- cycloalkyl;
- lower alkenyl;
- lower cycloalkenyl;
- halogen-substituted alkyl;
- amino-substituted alkyl;
- N-lower alkylamino-substituted alkyl;
- N,N-di-lower alkylamino-substituted alkyl;

- A 3
- carboxy-substituted alkylamino;
 - lower alkoxycarbonyl-substituted alkylamino;
 - phenyl-lower alkoxycarbonyl-substituted alkylamino;
 - -OR⁶;
 - -SR⁶;
 - -S(O)R⁶;
 - -S(O)₂R⁶;
 - halogenated lower alkoxy;
 - halogenated lower alkylthio;
 - halogenated lower alkylsulfonyl;
 - -OCOR⁶;
 - -COR⁶;
 - -CO₂R⁶;
 - -CON(R⁶)₂;
 - -CH₂OR³;
 - -NO₂;
 - -CN;
 - amidino;
 - guanidino;
 - sulfo;
 - -B(OH)₂;
 - optionally substituted aryl;
 - optionally substituted heteroaryl;
 - optionally substituted saturated heterocyclyl;
 - optionally substituted partially unsaturated heterocyclyl;
 - -OCO₂R³;
 - optionally substituted heteroarylalkyl;
 - optionally substituted heteroaryloxy;
 - -S(O)_p(optionally substituted heteroaryl);
 - optionally substituted heteroarylalkyloxy;
 - -S(O)_p(optionally substituted heteroarylalkyl);

- -CHO;
- -OCON(R⁶)₂ ;
- -NR³CO₂R⁶ ;
- -NR³CON(R⁶)₂
- fused ring-forming bridges attached to and connecting adjacent positions of ring J, said bridges having the structures:

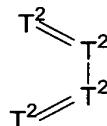
a)



wherein

each T² independently represents N, CH, or CG⁴;T³ represents S, O, CR⁴G⁴, C(R⁴)₂, or NR³; andbonding to ring J is achieved via terminal atoms T² and T³;

b)



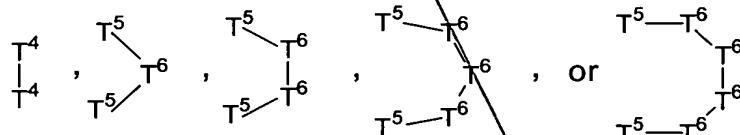
wherein

each T² independently represents N, CH, or CG⁴;with the proviso that a maximum of two bridge atoms T² may be N ;

and

bonding to ring J is achieved via terminal atoms T²; and

c)



wherein

each T⁴, T⁵, and T⁶ independently represents O, S, CR⁴G⁴, C(R⁴)₂, or NR³; andbonding to ring J is achieved via terminal atoms T⁴ or T⁵ ;

with the provisos that:

i) when one T⁴ is O, S, or NR³, the other T⁴ is CR⁴G⁴ or C(R⁴)₂ ;

- ii) a bridge comprising T⁵ and T⁶ atoms may contain a maximum of two heteroatoms O, S, or N; and
- iii) in a bridge comprising T⁵ and T⁶ atoms, when one T⁵ group and one T⁶ group are O atoms, or two T⁶ groups are O atoms, said O atoms are separated by at least one carbon atom;

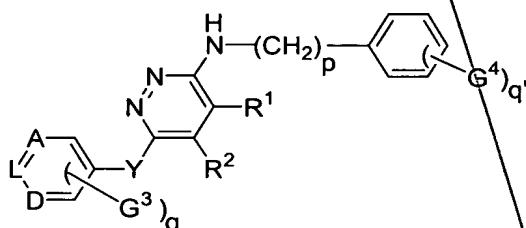
*Sub
B1
p3*

and with the further provisos that:

- in G¹, G², G³, and G⁴, when two groups R⁶ are each alkyl and located on the same N atom they may be linked by a bond, an O, an S, or NR³ to form a heterocycle of 5 – 7 ring atoms; and
- when an aryl, heteroaryl, or heterocyclyl ring is optionally substituted, that ring may bear up to 5 substituents which are independently selected from the group consisting of amino, mono-loweralkyl-substituted amino, di-loweralkyl-substituted amino, lower alkanoylamino, halogeno, lower alkyl, halogenated lower alkyl, hydroxy, lower alkoxy, lower alkylthio, halogenated lower alkoxy, halogenated lower alkylthio, lower alkanoyloxy, -CO₂R³, -CHO, -CH₂OR³, -OCO₂R³, -CON(R⁶)₂, -OCO N(R⁶)₂, -NR³CON(R⁶)₂, nitro, amidino, guanidino, mercapto, sulfo, and cyano;

or a pharmaceutically acceptable salt or prodrug thereof.

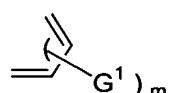
8. (amended) A compound having the structural formula



wherein

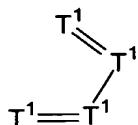
R¹ and R² :

- i) together form a bridge of structure



wherein bonding is achieved via the terminal carbon atoms; or

ii) together form a bridge of structure



wherein one of the ring members T^1 is N and the others are CH, and bonding is achieved via the terminal atoms; and

wherein

m is 0 or an integer 1 – 2; and

*G*¹ is a substituent independently selected from the group consisting of

- -N(R⁶)₂;
- -NR³COR⁶;
- halogen;
- alkyl;
- amino-substituted alkylamino;
- N-lower alkylamino-substituted alkylamino;
- N,N-di-lower alkylamino-substituted alkylamino;
- N-lower alkanoylamino-substituted alkylamino;
- hydroxy-substituted alkylamino;
- carboxy-substituted alkylamino;
- lower alkoxy carbonyl-substituted alkylamino;
- -OR⁶;
- -SR⁶;
- -S(O)R⁶;
- -S(O)₂R⁶;
- halogenated lower alkoxy;
- halogenated lower alkylthio;
- halogenated lower alkylsulfonyl;
- -OCOR⁶;
- -COR⁶;
- -CO₂R⁶;

- Sub B1*
- -CON(R⁶)₂;
 - -NO₂;
 - -CN;
 - optionally substituted heteroarylalkyl;
 - optionally substituted heteroaryloxy;
 - -S(O)_p(optionally substituted heteroaryl);
 - optionally substituted heteroarylalkyloxy;
 - -S(O)_p(optionally substituted heteroarylalkyl);

R³ is H or lower alkyl;

AB
R⁶ is independently selected from the group consisting of

- H;
- lower alkyl;
- optionally substituted aryl;
- optionally substituted aryl lower alkyl; and

p is 0 or 1;

Y is selected from the group consisting of

- lower alkylene, optionally substituted by OH or OAcyl;
- -CH₂-O-;
- -CH₂-S-;
- -CH₂-NH-;
- -O-;
- -S-;
- -NH-;
- -(CH₂)_n-S(O)_p-(5-membered heteroaryl)-(CH₂)_s-;
- -(CH₂)_n-C(G²)(H)-(CH₂)_s-;

wherein

n and s are each independently 0 or 1; and

G^2 is selected from the group consisting of $-CN$, $-CO_2R^3$, $-CON(R^6)_2$, and $-CH_2N(R^6)_2$;

- $-O-CH_2-$;
- $-S(O)-$;
- $-S(O)_2-$;
- $-SCH_2-$;
- $-S(O)CH_2-$;
- $-S(O)_2CH_2-$;
- $-CH_2S(O)-$; and
- $-CH_2S(O)_2-$

*Sub
B1*

A3
A and D independently represent N or CH;

L represents N or CH;

with the provisos that

- a) the total number of N atoms in the ring containing A, D, and L is 1 or 2; and
- b) when L represents CH, at least one of A and D is an N atom;

q is 0, 1, or 2;

G^3 is selected from the group consisting of

- $-NR^3COR^6$;
- $-OR^6$;
- $-SR^6$;
- $-S(O)R^6$;
- $-S(O)_2R^6$;
- $-CO_2R^6$;
- $-CON(R^6)_2$;
- $-S(O)_2N(R^6)_2$;
- $-CN$;
- optionally substituted aryl;
- optionally substituted heteroaryl;

- optionally substituted heteroarylalkyl;
- optionally substituted heteroaryloxy;
- $-S(O)_p$ (optionally substituted heteroaryl);
- optionally substituted heteroarylalkyloxy;
- $-S(O)_p$ (optionally substituted heteroarylalkyl);

q' represents the number of substituents G^4 on the phenyl ring and is 0, 1, 2, or 3;

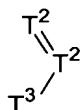
and

G^4 moieties are selected from the group consisting of

- Sub B1 A3*
- $-N(R^6)_2$;
 - $-NR^3COR^6$;
 - halogen;
 - alkyl;
 - halogen-substituted alkyl;
 - hydroxy-substituted alkyl;
 - carboxy-substituted alkyl;
 - lower alkoxy carbonyl-substituted alkyl;
 - amino-substituted alkylamino;
 - N-lower alkylamino-substituted alkylamino;
 - N,N-di-lower alkylamino-substituted alkylamino;
 - N-lower alkanoylamino-substituted alkylamino;
 - hydroxy-substituted alkylamino;
 - carboxy-substituted alkylamino;
 - lower alkoxy carbonyl-substituted alkylamino;
 - phenyl-lower alkoxy carbonyl-substituted alkylamino;
 - $-OR^6$;
 - $-SR^6$;
 - $-S(O)R^6$;
 - $-S(O)_2R^6$;
 - halogenated lower alkoxy;
 - halogenated lower alkylthio;

- Sub B1
P/B*
- halogenated lower alkylsulfonyl;
 - -OCOR⁶;
 - -COR⁶;
 - -CO₂R⁶;
 - -CON(R⁶)₂;
 - -CH₂OR³;
 - -NO₂;
 - -CN;
 - optionally substituted heteroarylalkyl;
 - optionally substituted heteroaryloxy;
 - -S(O)_p(optionally substituted heteroaryl);
 - optionally substituted heteroarylalkyloxy;
 - -S(O)_p(optionally substituted heteroarylalkyl);
 - fused ring-forming bridges attached to and connecting adjacent positions of the phenyl ring, said bridges having the structures:

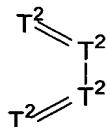
a)



wherein

each T² independently represents N, CH, or CG⁴;T³ represents S, O, CHG⁴, C(H)₂, or NR³; andbonding to the phenyl ring is achieved via terminal atoms T² and T³;

b)



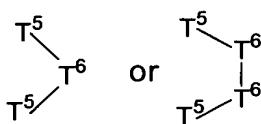
wherein

each T² independently represents N, CH, or CG⁴;with the proviso that a maximum of two bridge atoms T² may be N ;

and

bonding to the phenyl ring is achieved via terminal atoms T²; and

c)



wherein

each T^5 , and T^6 independently represents O, S, CHG^4 , $\text{C}(\text{H})_2$, or NR^3 ;
and

bonding to the phenyl ring is achieved via terminal atoms T^5 ;

with the provisos that:

- Sub B1*
- A/S*
- i) a bridge comprising T^5 and T^6 atoms may contain a maximum of two heteroatoms O, S, or N; and
 - ii) in a bridge comprising T^5 and T^6 atoms, when one T^5 group and one T^6 group are O atoms, or two T^6 groups are O atoms, said O atoms are separated by at least one carbon atom;

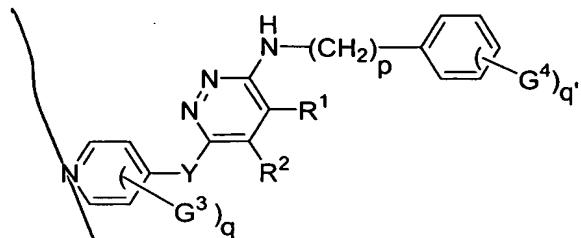
and with the further provisos that:

- in G^1 , G^2 , G^3 , and G^4 , when two groups R^6 are each alkyl and located on the same N atom they may be linked by a bond, an O, an S, or NR^3 to form a heterocycle of 5 – 7 ring atoms; and

- when an aryl, heteroaryl, or heterocyclyl ring is optionally substituted, that ring may bear up to 2 substituents which are independently selected from the group consisting of amino, mono-loweralkyl-substituted amino, di-loweralkyl-substituted amino, lower alkanoylamino, halogeno, lower alkyl, halogenated lower alkyl, hydroxy, lower alkoxy, lower alkylthio, halogenated lower alkoxy, halogenated lower alkylthio, lower alkanoyloxy, $-\text{CO}_2\text{R}^3$, $-\text{CH}_2\text{OR}^3$, $-\text{OCO}_2\text{R}^3$, $-\text{CON}(\text{R}^6)_2$, $-\text{OCO}\text{N}(\text{R}^6)_2$, $-\text{NR}^3\text{CON}(\text{R}^6)_2$, nitro, and cyano;

or a pharmaceutically acceptable salt or prodrug thereof.

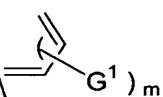
9. (amended) A compound having the structural formula



wherein

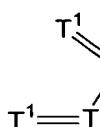
R^1 and R^2 :

- i) together form a bridge of structure



wherein bonding is achieved via the terminal carbon atoms, and any group G^1 is located on a non-terminal atom of the bridge; or

- ii) together form a bridge of structure



wherein one of the ring members T^1 is N and the others are CH, and bonding is achieved via the terminal atoms; and

wherein

m is 0 or an integer 1–2; and

G^1 is a substituent independently selected from the group consisting of

- $-N(R^6)_2$;
- $-NR^3COR^6$;
- halogen;
- $-OR^6$ wherein R^6 represents lower alkyl;
- $-NO_2$;
- optionally substituted heteroaryloxy;
- optionally substituted heteroarylalkyloxy;

R^3 is H or lower alkyl;

R^6 is independently selected from the group consisting of

- H;
- lower alkyl;
- optionally substituted aryl;
- optionally substituted aryl lower alkyl; and

*Sub
h1*

p is 0 or 1;

Y is selected from the group consisting of

- lower alkylene, optionally substituted by OH;
- $-\text{CH}_2\text{O}-$;
- $-\text{S}-$;
- $-\text{NH}-$;
- $-\text{S}(\text{O})_p(5\text{-membered heteroaryl})-$;
- $-\text{C}(\text{CN})(\text{H})-$;
- $-\text{O}-\text{CH}_2-$;
- $-\text{S}(\text{O})-$; and
- $-\text{S}(\text{O})_2-$;

q is 0 or 1;

G^3 is selected from the group consisting of

- $-\text{NR}^3\text{COR}^6$;
- $-\text{CO}_2\text{R}^6$;
- $-\text{CON}(\text{R}^6)_2$;
- $-\text{S}(\text{O})_2\text{N}(\text{R}^6)_2$;

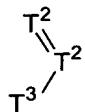
q' represents the number of substituents G^4 on the phenyl ring and is 0, 1, 2, or 3;
and

G^4 moieties are selected from the group consisting of

- $-\text{N}(\text{R}^6)_2$;

- Sub B1*
- A3*
- halogen;
 - lower alkyl;
 - halogen-substituted lower alkyl;
 - -OR⁶;
 - -SR⁶;
 - -S(O)R⁶;
 - -S(O)₂R⁶;
 - halogenated lower alkoxy;
 - halogenated lower alkylthio;
 - halogenated lower alkylsulfonyl;
 - -OCOR⁶;
 - -COR⁶;
 - -CO₂R⁶;
 - -CON(R⁶)₂;
 - -CH₂OR³;
 - -NO₂;
 - -CN;
 - optionally substituted heteroarylalkyl;
 - optionally substituted heteroaryloxy;
 - -S(O)_p(optionally substituted heteroaryl);
 - optionally substituted heteroarylalkyloxy;
 - -S(O)_p(optionally substituted heteroarylalkyl);
 - fused ring-forming bridges attached to and connecting adjacent positions of the phenyl ring, said bridges having the structures:

a)



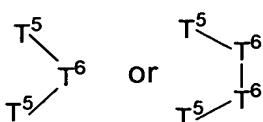
wherein

each T² independently represents N, CH, or CG⁴;

T³ represents S, O, CHG⁴, CH₂, or NR³; and

bonding to the phenyl ring is achieved via terminal atoms T² and T³;

b)



wherein

each T⁵, and T⁶ independently represents O, S, CHG⁴, CH₂, or NR³; and bonding to the phenyl ring is achieved via terminal atoms T⁵; with the provisos that:

- Sub b1*
- A/B*
- i) a bridge comprising T⁵ and T⁶ atoms may contain a maximum of two heteroatoms O, S, or N; and
 - ii) in a bridge comprising T⁵ and T⁶ atoms, when one T⁵ group and one T⁶ group are O atoms, or two T⁶ groups are O atoms, said O atoms are separated by at least one carbon atom;

and with the further provisos that:

- in G¹, G², G³, and G⁴, when two groups R⁶ are each alkyl and located on the same N atom they may be linked by a bond, an O, an S, or NR³ to form a heterocycle of 5 – 6 ring atoms; and

- when an aryl, heteroaryl, or heterocyclyl ring is optionally substituted, that ring may bear up to 2 substituents which are independently selected from the group consisting of amino, mono-loweralkyl-substituted amino, di-loweralkyl-substituted amino, lower alkanoylamino, halogeno, lower alkyl, halogenated lower alkyl, hydroxy, lower alkoxy, lower alkylthio, halogenated lower alkoxy, halogenated lower alkylthio, -CO₂R³, -CON(R⁶)₂, nitro, and cyano;

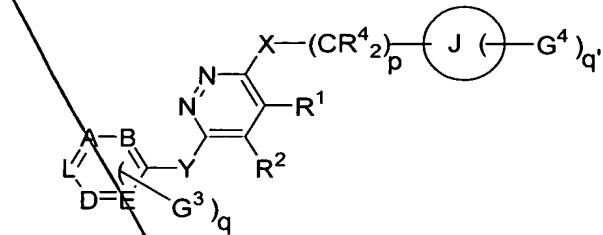
or a pharmaceutically acceptable salt or prodrug thereof.

Sub b1

11. (Amended) A method of treating a mammal having a condition of tumor growth, retinopathy, rheumatoid arthritis, psoriasis, or a bullous disorder associated with subepidermal blister formation, comprising administering to said mammal an amount of a compound of claim 7 which is effective to treat said condition.

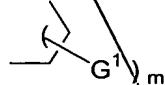
12. (cancelled) The method of claim 11, wherein said condition is tumor growth; retinopathy, including diabetic retinopathy, ischemic retinal-vein occlusion, retinopathy of prematurity, and age-related macular degeneration; rheumatoid arthritis; psoriasis; or a bullous disorder associated with subepidermal blister formation, including bullous pemphigoid, erythema multiforme, and dermatitis herpetiformis.

13. (amended) A compound having the structural formula



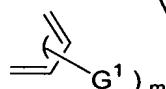
R¹ and R² :

- i) independently represent H or lower alkyl;
- ii) together form a bridge of structure



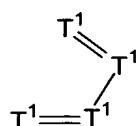
wherein bonding is achieved via the terminal carbon atoms;

- iii) together form a bridge of structure



wherein bonding is achieved via the terminal carbon atoms; or

- iv) together form a bridge of structure



wherein one or two ring members T¹ are N and the others are CH, and bonding is achieved via the terminal atoms; and

wherein

m is 0 or an integer 1 – 4; and

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G^1 is a substituent independently selected from the group consisting of

- $-N(R^6)_2$;
- $-NR^3COR^6$;
- halogen;
- alkyl;
- cycloalkyl;
- lower alkenyl;
- lower cycloalkenyl;
- halogen-substituted alkyl;
- amino-substituted alkyl;
- N-lower alkylamino-substituted alkyl;
- N,N-di-lower alkylamino-substituted alkyl;
- N-lower alkanoylamino-substituted alkyl;
- hydroxy-substituted alkyl;
- cyano-substituted alkyl;
- carboxy-substituted alkyl;
- lower alkoxycarbonyl-substituted alkyl;
- phenyl lower alkoxycarbonyl-substituted alkyl;
- halogen-substituted alkylamino;
- amino-substituted alkylamino;
- N-lower alkylamino-substituted alkylamino;
- N,N-di-lower alkylamino-substituted alkylamino;
- N-lower alkanoylamino-substituted alkylamino;
- hydroxy-substituted alkylamino;
- cyano-substituted alkylamino;
- carboxy-substituted alkylamino;
- lower alkoxycarbonyl-substituted alkylamino;
- phenyl-lower alkoxycarbonyl-substituted alkylamino;
- $-OR^6$;
- $-SR^6$;
- $-S(O)R^6$;

- Su b
B1*
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- -S(O)₂R⁶;
 - halogenated lower alkoxy;
 - halogenated lower alkylthio;
 - halogenated lower alkylsulfonyl;
 - -OCOR⁶;
 - -COR⁶;
 - -CO₂R⁶;
 - -CON(R⁶)₂;
 - -CH₂OR³;
 - -NO₂;
 - -CN;
 - amidino;
 - guanidino;
 - sulfo;
 - -B(OH)₂;
 - optionally substituted aryl;
 - optionally substituted heteroaryl;
 - optionally substituted saturated heterocyclyl;
 - optionally substituted partially unsaturated heterocyclyl;
 - -OCO₂R³;
 - optionally substituted heteroarylalkyl;
 - optionally substituted heteroaryloxy;
 - -S(O)_p(optionally substituted heteroaryl);
 - optionally substituted heteroarylalkyloxy;
 - -S(O)_p(optionally substituted heteroarylalkyl);
 - -CHO;
 - -OCON(R⁶)₂;
 - -NR³CO₂R⁶;
 - -NR³CON(R⁶)₂

R³ is H or lower alkyl;

Sub B1

R^6 is independently selected from the group consisting of

- H;
- alkyl;
- optionally substituted aryl;
- optionally substituted aryl lower alkyl; and

A5

R^4 is H, halogen, or lower alkyl;

p is 0, 1, or 2;

X is selected from the group consisting of O, S, and NH;

Y is selected from the group consisting of

- lower alkylene, optionally substituted by OH or OAcyl;
- $-CH_2-O-$;
- $-CH_2-S-$;
- $-CH_2-NH-$;
- $-O-$;
- $-S-$;
- $-NH-$;
- $-(CR^4_2)_n-S(O)_p-(5\text{-membered heteroaryl})-(CR^4_2)_s-$;
- $-(CR^4_2)_n-C(G^2)(R^4)-(CR^4_2)_s-$;

wherein

n and s are each independently 0 or an integer of 1 – 2; and

G^2 is selected from the group consisting of $-CN$, $-CO_2R^3$, $-CON(R^6)_2$, and
 $-CH_2N(R^6)_2$;

- $-O-CH_2-$;
- $-S(O)-$;
- $-S(O)_2-$;
- $-SCH_2-$;
- $-S(O)CH_2-$;

- -S(O)₂CH₂- ;
- -CH₂S(O)- ; and
- -CH₂S(O)₂-

A and D independently represent N or CH;

B and E independently represent N or CH;

L represents N or CH;

with the provisos that

- a) the total number of N atoms in the ring containing A, B, D, E, and L is 1, 2, or 3;
and
- b) when L represents CH, at least one of A and D is an N atom;

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q is 0, 1, or 2;

G³ is selected from the group consisting of

- lower alkyl;
- -NR³COR⁶;
- carboxy-substituted alkyl;
- lower alkoxy carbonyl-substituted alkyl;
- -OR⁶;
- -SR⁶;
- -S(O)R⁶;
- -S(O)₂R⁶;
- -OCOR⁶;
- -COR⁶;
- -CO₂R⁶;
- -CH₂OR³;
- -CON(R⁶)₂ ;
- -S(O)₂N(R⁶)₂ ;
- -NO₂;
- -CN;

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- optionally substituted aryl;
 - optionally substituted heteroaryl;
 - optionally substituted saturated heterocycl;
 - optionally substituted partially unsaturated heterocycl;
 - optionally substituted heteroarylalkyl;
 - optionally substituted heteroaryloxy;
 - $-S(O)_p$ (optionally substituted heteroaryl);
 - optionally substituted heteroarylalkyloxy;
 - $-S(O)_p$ (optionally substituted heteroarylalkyl);
 - $-OCON(R^6)_2$;
 - $-NR^3CO_2R^6$;
 - $-NR^3CON(R^6)_2$;
- AS*

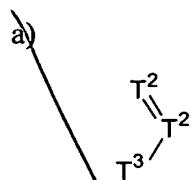
J is a ring selected from the group consisting of

- aryl;
- pyridyl; and
- cycloalkyl;

q' represents the number of substituents G^4 on ring J and is 0, 1, 2, 3, 4, or 5, and

G^4 moieties are selected from the group consisting of

- optionally substituted heteroarylalkyl;
- optionally substituted heteroaryloxy;
- $-S(O)_p$ (optionally substituted heteroaryl);
- optionally substituted heteroarylalkyloxy;
- $-S(O)_p$ (optionally substituted heteroarylalkyl);
- $-CHO$;
- $-OCON(R^6)_2$;
- $-NR^3CO_2R^6$;
- $-NR^3CON(R^6)_2$
- fused ring-forming bridges attached to and connecting adjacent positions of ring J, said bridges having the structures:

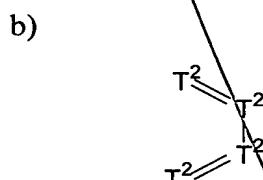


wherein

each T^2 independently represents N, CH, or CG^4 ;

T^3 represents S, O, CR^4G^4 , $C(R^4)_2$, or NR^3 ; and

bonding to ring J is achieved via terminal atoms T^2 and T^3 ;



wherein

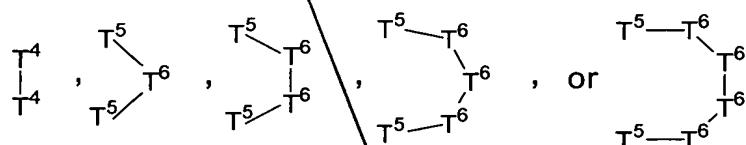
each T^2 independently represents N, CH, or CG^4 ;

with the proviso that a maximum of two bridge atoms T^2 may be N;

and

bonding to ring J is achieved via terminal atoms T^2 ; and

c)



wherein

each T^4 , T^5 , and T^6 independently represents O, S, CR^4G^4 , $C(R^4)_2$, or NR^3 ; and

bonding to ring J is achieved via terminal atoms T^4 or T^5 ;

with the provisos that:

- i) when one T^4 is O, S, or NR^3 , the other T^4 is CR^4G^4 or $C(R^4)_2$;
- ii) a bridge comprising T^5 and T^6 atoms may contain a maximum of two heteroatoms O, S, or N; and
- iii) in a bridge comprising T^5 and T^6 atoms, when one T^5 is O, the other T^5 is S, CR^4G^4 , $C(R^4)_2$ or NR^3 ;

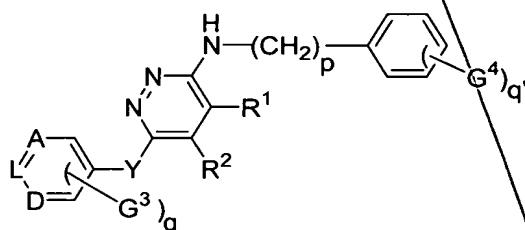
iv) in a bridge comprising T⁵ and T⁶ atoms, when one T⁵ group and one T⁶ group are O atoms, or two T⁶ groups are O atoms, said O atoms are separated by at least one carbon atom;

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and with the further provisos that:

- in G¹, G², G³, and G⁴, when two groups R⁶ are each alkyl and located on the same N atom they may be linked by a bond, an O, an S, or NR³ to form a heterocycle of 5 – 7 ring atoms; and
 - when an aryl, heteroaryl, or heterocyclyl ring is optionally substituted, that ring may bear up to 5 substituents which are independently selected from the group consisting of amino, mono-loweralkyl-substituted amino, di-loweralkyl-substituted amino, lower alkanoylamino, halogeno, lower alkyl, halogenated lower alkyl, hydroxy, lower alkoxy, lower alkylthio, halogenated lower alkoxy, halogenated lower alkylthio, lower alkanoyloxy, -CO₂R³, -CHO, -CH₂OR³, -OCO₂R³, -CON(R⁶)₂, -OCO N(R⁶)₂, -NR³CON(R⁶)₂, nitro, amidino, guanidino, mercapto, sulfo, and cyano;
- or a pharmaceutically acceptable salt or prodrug thereof.

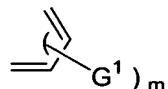
14. (amended) A compound having the structural formula



wherein

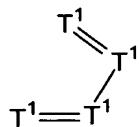
R¹ and R²:

- i) together form a bridge of structure



wherein bonding is achieved via the terminal carbon atoms; or

- ii) together form a bridge of structure



wherein one of the ring members T^1 is N and the others are CH, and bonding is achieved via the terminal atoms; and

wherein

m is 0 or an integer 1 – 2; and

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G^1 is a substituent independently selected from the group consisting of

- $-N(R^6)_2$;
- $-NR^3COR^6$;
- halogen;
- alkyl;
- amino-substituted alkylamino;
- N-lower alkylamino-substituted alkylamino;
- N,N-di-lower alkylamino-substituted alkylamino;
- N-lower alkanoylamino-substituted alkylamino;
- hydroxy-substituted alkylamino;
- carboxy-substituted alkylamino;
- lower alkoxy carbonyl-substituted alkylamino;
- $-OR^6$;
- $-SR^6$;
- $-S(O)R^6$;
- $-S(O)_2R^6$;
- halogenated lower alkoxy;
- halogenated lower alkylthio;
- halogenated lower alkylsulfonyl;
- $-OCOR^6$;
- $-COR^6$;
- $-CO_2R^6$;
- $-CON(R^6)_2$;

- -NO₂;
- -CN;
- optionally substituted heteroarylalkyl;
- optionally substituted heteroaryloxy;
- -S(O)_p(optionally substituted heteroaryl);
- optionally substituted heteroarylalkyloxy;
- -S(O)_p(optionally substituted heteroarylalkyl);

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R³ is H or lower alkyl;

R⁶ is independently selected from the group consisting of

- H;
- lower alkyl;
- optionally substituted aryl;
- optionally substituted aryl lower alkyl; and

p is 0 or 1;

Y is selected from the group consisting of

- lower alkylene, optionally substituted by OH or OAcyl;
 - -CH₂-O-;
 - -CH₂-S-;
 - -CH₂-NH-;
 - -O-;
 - -S-;
 - -NH-;
 - -(CH₂)_n-S(O)_p-(5-membered heteroaryl)-(CH₂)_s-;
 - -(CH₂)_n-C(G²)(H)-(CH₂)_s-;
- wherein

n and s are each independently 0 or 1; and

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G² is selected from the group consisting of -CN, -CO₂R³, -CON(R⁶)₂, and -CH₂N(R⁶)₂;

- -O-CH₂-;
- -S(O)-;
- -S(O)₂-;
- -SCH₂-;
- -S(O)CH₂-;
- -S(O)₂CH₂-;
- -CH₂S(O)-; and
- -CH₂S(O)₂-

AS

A and D independently represent N or CH;

L represents N or CH;

with the provisos that

- a) the total number of N atoms in the ring containing A, D, and L is 1 or 2; and
- b) when L represents CH, at least one of A and D is an N atom;

q is 0, 1, or 2;

G³ is selected from the group consisting of

- lower alkyl;
- -NR³COR⁶;
- -OR⁶;
- -SR⁶;
- -S(O)R⁶;
- -S(O)₂R⁶;
- -CO₂R⁶;
- -CON(R⁶)₂;
- -S(O)₂N(R⁶)₂;
- -CN;
- optionally substituted aryl;

- optionally substituted heteroaryl;
- optionally substituted heteroarylalkyl;
- optionally substituted heteroaryloxy;
- $-S(Q)_p$ (optionally substituted heteroaryl);
- optionally substituted heteroarylalkyloxy;
- $-S(O)_p$ (optionally substituted heteroarylalkyl);

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β1*

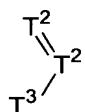
q' represents the number of substituents G^4 on the phenyl ring and is 0, 1, 2, or 3;

and

G^4 moieties are selected from the group consisting of

- optionally substituted heteroarylalkyl;
- optionally substituted heteroaryloxy;
- $-S(O)_p$ (optionally substituted heteroaryl);
- optionally substituted heteroarylalkyloxy;
- $-S(O)_p$ (optionally substituted heteroarylalkyl);
- fused ring-forming bridges attached to and connecting adjacent positions of the phenyl ring, said bridges having the structures:

a)



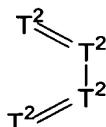
wherein

each T^2 independently represents N, CH, or CG^4 ;

T^3 represents S, O, CHG^4 , $C(H)_2$, or NR^3 ; and

bonding to the phenyl ring is achieved via terminal atoms T^2 and T^3 ;

b)



wherein

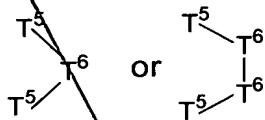
each T^2 independently represents N, CH, or CG^4 ;

with the proviso that a maximum of two bridge atoms T^2 may be N ;

and

bonding to the phenyl ring is achieved via terminal atoms T^2 ; and

c)



wherein

each T^5 , and T^6 independently represents O, S, CHG⁴, CH₂, or NR³; and

bonding to the phenyl ring is achieved via terminal atoms T^5 ;

with the provisos that:

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- i) a bridge comprising T^5 and T^6 atoms may contain a maximum of two heteroatoms O, S, or N; and
 - ii) in a bridge comprising T^5 and T^6 atoms, when one T^5 is O, the other T^5 is S, CHG⁴, CH₂ or NR³;
 - iii) in a bridge comprising T^5 and T^6 atoms, when one T^5 group and one T^6 group are O atoms, or two T^6 groups are O atoms, said O atoms are separated by at least one carbon atom;

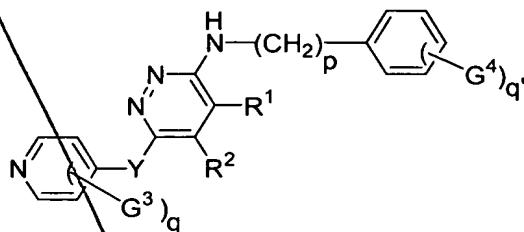
and with the further provisos that:

- in G¹, G², G³, and G⁴, when two groups R⁶ are each alkyl and located on the same N atom they may be linked by a bond, an O, an S, or NR³ to form a heterocycle of 5 – 7 ring atoms; and

- when an aryl, heteroaryl, or heterocyclyl ring is optionally substituted, that ring may bear up to 2 substituents which are independently selected from the group consisting of amino, mono-loweralkyl-substituted amino, di-loweralkyl-substituted amino, lower alkanoyl amino, halogeno, lower alkyl, halogenated lower alkyl, hydroxy, lower alkoxy, lower alkylthio, halogenated lower alkoxy, halogenated lower alkylthio, lower alkanoyloxy, -CO₂R³, -CH₂OR³, -OCO₂R³, -CON(R⁶)₂, -OCO N(R⁶)₂, -NR³CON(R⁶)₂, nitro, and cyano;

or a pharmaceutically acceptable salt or prodrug thereof.

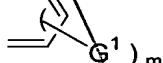
15. (amended) A compound having the structural formula



wherein

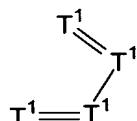
R¹ and R²:

- i) together form a bridge of structure



wherein bonding is achieved via the terminal carbon atoms, and any group G¹ is located on a non-terminal atom of the bridge; or

- ii) together form a bridge of structure



wherein one of the ring members T¹ is N and the others are CH, and bonding is achieved via the terminal atoms; and

wherein

m is 0 or an integer 1 – 2; and

G¹ is a substituent independently selected from the group consisting of

- -N(R⁶)₂;
- -NR³COR⁶;
- halogen;
- -OR⁶ wherein R⁶ represents lower alkyl;
- -NO₂;
- optionally substituted heteroaryloxy;
- optionally substituted heteroarylalkyloxy;

R³ is H or lower alkyl;

R⁶ is independently selected from the group consisting of

- H;
- lower alkyl;
- optionally substituted aryl;
- optionally substituted aryl lower alkyl; and

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p is 0 or 1;

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Y is selected from the group consisting of

- lower alkylene, optionally substituted by OH;
- -CH₂-O- ;
- -S- ;
- -NH- ;
- -S(O)_p-(5-membered heteroaryl)-;
- -C(CN)(H)- ;
- -O-CH₂- ;
- -S(O)- ; and
- -S(O)₂- ;

q is 0 or 1;

G³ is selected from the group consisting of

- lower alkyl;
- -NR³COR⁶;
- -CO₂R⁶;
- -CON(R⁶)₂ ;
- -S(O)₂N(R⁶)₂ ;

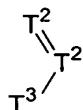
q' represents the number of substituents G⁴ on the phenyl ring, and is 0, 1, 2, or 3;

and

G⁴ moieties are selected from the group consisting of

- optionally substituted heteroarylalkyl;
- optionally substituted heteroaryloxy;
- -S(O)_p(optionally substituted heteroaryl);
- optionally substituted heteroarylalkyloxy;
- -S(O)_p(optionally substituted heteroarylalkyl);
- fused ring-forming bridges attached to and connecting adjacent positions of the phenyl ring, said bridges having the structures:

a)



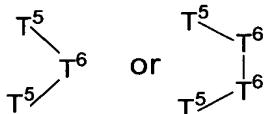
wherein

each T² independently represents N, CH, or CG⁴;

T³ represents S, O, CHG⁴, CH₂, or NR³; and

bonding to the phenyl ring is achieved via terminal atoms T² and T³;

b)



wherein

each T⁵, and T⁶ independently represents O, S, CHG⁴, CH₂, or NR³; and bonding to the phenyl ring is achieved via terminal atoms T⁵;

with the provisos that:

- i) a bridge comprising T⁵ and T⁶ atoms may contain a maximum of two heteroatoms O, S, or N; and
- ii) in a bridge comprising T⁵ and T⁶ atoms, when one T⁵ is O, the other T⁵ is S, CR⁴G⁴, C(R⁴)₂ or NR³;
- iii) in a bridge comprising T⁵ and T⁶ atoms, when one T⁵ group and one T⁶ group are O atoms, or two T⁶ groups are O atoms, said O atoms are separated by at least one carbon atom;

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and with the further provisos that:

- in G¹, G², G³, and G⁴, when two groups R⁶ are each alkyl and located on the same N atom they may be linked by a bond, an O, an S, or NR³ to form a heterocycle of 5 – 6 ring atoms; and
 - when an aryl, heteroaryl, or heterocyclyl ring is optionally substituted, that ring may bear up to 2 substituents which are independently selected from the group consisting of amino, mono-loweralkyl-substituted amino, di-loweralkyl-substituted amino, lower alkanoylamino, halogeno, lower alkyl, halogenated lower alkyl, hydroxy, lower alkoxy, lower alkylthio, halogenated lower alkoxy, halogenated lower alkylthio, -CO₂R³, -CON(R⁶)₂, nitro, and cyano;
- AS'*
- or a pharmaceutically acceptable salt or prodrug thereof.
-

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17. (Amended) A method of treating a mammal having a condition of tumor growth, retinopathy, rheumatoid arthritis, psoriasis, or a bullous disorder associated with subepidermal blister formation, comprising administering to said mammal an amount of a compound of claim 13 which is effective to treat said condition.

18. (Cancelled) The method of claim 17, wherein said condition is tumor growth; retinopathy, including diabetic retinopathy, ischemic retinal-vein occlusion, retinopathy of prematurity, and age-related macular degeneration; rheumatoid arthritis; psoriasis; or a bullous disorder associated with subepidermal blister formation, including bullous pemphigoid, erythema multiforme, and dermatitis herpetiformis.

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19. (Amended) A compound selected from the group consisting of:

- a) 4-[4-(4-Chlorophenylamino)phthalazin-1-ylmethyl]pyridin-2-yl carboxylic acid methylamide;
 - b) 4-[4-(4-Chlorophenylamino)phthalazin-1-ylmethyl]pyridin-2-yl carboxylic acid amide;
 - c) 1-(4-chlorophenylamino)-4-(3-pyridylmethoxy)phthalazine;
 - d) 4-[4-(4-Chlorophenylamino)phthalazin-1-yloxymethyl]pyridin-2-yl carboxylic acid methylamide;
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- e) 4-[4-(4-Chlorophenylamino)phthalazin-1-yloxymethyl]pyridin-2-yl carboxylic acid amide;
 - f) 4-[4-(3-Bromophenylamino)phthalazin-1-ylmethyl]-pyridin-2-yl carboxylic acid methylamide;
 - g) 4-[4-(3-Bromophenylamino)phthalazin-1-ylmethyl]-pyridin-2-yl carboxylic acid amide;
 - h) 1-(4-chlorophenylamino)-4-[(2-phenyl-4-pyridyl)methyl]phthalazine;
 - i) 1-[4-(4-pyridyloxy)phenylamino]-4-(4-pyridylmethyl)phthalazine;
 - j) 1-(indan-5-ylamino)-4-(4-pyridylmethyl)phthalazine;
 - k) 4-[4-(4-Chlorophenylamino)phthalazin-1-ylmethyl]pyridin-2-yl carboxylic acid methylamide dihydrochloride;
 - l) 4-[4-(4-Chlorophenylamino)phthalazin-1-ylmethyl]pyridin-2-yl carboxylic acid methylamide dimethanesulfonate;
 - m) 4-[4-(4-Chlorophenylamino)phthalazin-1-ylmethyl]pyridin-2-yl carboxylic acid amide dihydrochloride;
 - n) 4-[4-(4-Chlorophenylamino)phthalazin-1-ylmethyl]pyridin-2-yl carboxylic acid amide dimethanesulfonate;
 - o) 4-[4-(4-Chlorophenylamino)phthalazin-1-yloxymethyl]pyridin-2-yl carboxylic acid amide dihydrochloride;
 - p) 4-[4-(4-Chlorophenylamino)phthalazin-1-yloxymethyl]pyridin-2-yl carboxylic acid amide dimethanesulfonate;
 - q) 1-(4-chlorophenylamino)-4-[5-(4-pyridyl)-1H-1,2,4-triazolyl-3-ylthio]phthalazine;
 - r) 1-(4-isopropylphenylamino)-4-[5-(4-pyridyl)-1H-1,2,4-triazolyl-3-ylthio]phthalazine
 - s) 1-(4-chlorophenylamino)-4-(4-pyridylsufonyl)phthalazine;
 - t) 1-(4-chlorophenylamino)-4-(4-pyridylsufinyl)phthalazine;
 - v) 1-(indan-5-ylamino)-4-(4-pyridylcyanomethyl)phthalazine; and
 - w) 1-(benzothiazol-6-ylamino)-4-(4-pyridylcyanomethyl)phthalazine.

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20. (New) The method of claim 5, wherein said condition of retinopathy is diabetic retinopathy, ischemic retinal-vein occlusion, retinopathy of prematurity, or age-related macular degeneration.

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21. (New) The method of claim 5, wherein when said condition is a bullous disorder associated with subepidermal blister formation, it is bullous pemphigoid, erythema multiforme, or dermatitis herpetiformis.
 22. (New) The method of claim 11, wherein said condition of retinopathy is diabetic retinopathy, ischemic retinal-vein occlusion, retinopathy of prematurity, or age-related macular degeneration.
 23. (New) The method of claim 11, wherein when said condition is a bullous disorder associated with subepidermal blister formation, it is bullous pemphigoid, erythema multiforme, or dermatitis herpetiformis.
 24. (New) The method of claim 17, wherein said condition of retinopathy is diabetic retinopathy, ischemic retinal-vein occlusion, retinopathy of prematurity, or age-related macular degeneration.
 25. (New) The method of claim 17, wherein when said condition is a bullous disorder associated with subepidermal blister formation, it is bullous pemphigoid, erythema multiforme, or dermatitis herpetiformis.

Remarks / Arguments

As a result of this amendment, claims 1-5, 7-11, 13-17, and 19-25 are pending in the application. Claims 6, 12, and 18 have been cancelled. New claims 20-25 have been added. No new matter has been added.

Rejections under §112, second paragraph

The examiner rejected claims 1-19 under §112, second paragraph as being indefinite for several reasons.

In paragraph 1 of the official action, the examiner refers to the word "generalized" in claims 1-3, 7-9, and 13-15 and asserts it renders the claims vague and indefinite, stating